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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/562,494

04/27/2006

Benjamin Oshlack

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EXAMINER

CLAYTOR, DEIRDRE RENEE

ART UNIT

PAPER NUMBER

1627

MAIL DATE

DELIVERY MODE

06/24/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/562,494	Applicant(s) OSHLACK ET AL.	
	Examiner Renee Claytor	Art Unit 1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/25/2010, 3/16/2010</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/25/2010 has been entered.

Response to Arguments

Applicants argue over the 35 USC 103 rejection over Oshlack et al. (US PgPub 2003/0229111). In particular, Applicants argue that there is no teaching in the cited reference that would support the conclusion that those skilled in the art would consider it obvious to optimize the compositions described in the cited reference by lowering naltrexone to hydrocodone ratio. Applicants point to the Examples of the Oshlack et al. reference which teaches ratios that do not fall within what is presently claimed.

In response to applicant's argument that there is no teaching in the cited reference that would support the conclusion that those skilled in the art would consider it obvious to optimize the compositions described in the cited reference by lowering naltrexone to hydrocodone ratio, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

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See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Furthermore, Oshlack does not have to exemplify each and every embodiment of the invention. Oshlack teaches amounts of naltrexone in amounts of greater than 0.001 mg and less than 20 mg and amounts of hydrocodone between 5 and 20 mg. Oshlack teaches that in certain embodiments the composition comprises 5-20 mg of hydrocodone and less than 5 mg of naltrexone. Accordingly, if naltrexone is in a dose of 0.056 mg and hydrocodone is 5 mg, then the ratio is 0.011:1. Therefore, Oshlack et al. teach dosage ranges that would fall in the ratios as presently claimed. Because Oshlack et al. teach dosage ranges of the compositions that fall within the ratios claimed, it would be desirable to optimize a dosage range between the two compositions to effectively treat pain. Accordingly, it is deemed that the rejection is proper and is maintained below.

Applicants present arguments over the 35 USC 103 rejection over Sherman et al. (US PgPub 2003/0191147) in view of Kaiko et al. (US PgPub 2003/0031712). In particular, Applicant's argue that neither Sherman et al. or Kaiko et al. teach the claims ratio of naltrexone to oxycodone. Applicants point to specific examples in the Sherman and Kaiko et al. references that teach ratios of hydrocodone and naltrexone that are higher than that claimed. Applicants also argue that there is no teaching in the cited references that would support the conclusion that those skilled in the art would consider it obvious to optimize the compositions described in the cited reference by lowering naltrexone to hydrocodone ratio.

In response to applicant's argument that there is no teaching in the cited reference that would support the conclusion that those skilled in the art would consider it

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obvious to optimize the compositions described in the cited reference by lowering naltrexone to hydrocodone ratio, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Furthermore, the prior art does not have to exemplify each and every embodiment of the invention. Sherman et al. teaches ranges of naltrexone with a minimum amount being 0.055 mg to 0.56 mg (paragraphs 0061 and 0063). Further, Sherman teaches that hydrocodone is present in a range of 0.1 to 300 mg (paragraphs 0071-0072). Sherman further exemplifies a composition in the claimed ratio. Sherman et al. teach dosage ranges of the compositions that fall within the ratios claimed, it would be desirable to optimize a dosage range between the two compositions to effectively treat pain. Accordingly, it is deemed that the rejection is proper and is maintained below.

Due to Applicant's amendments, please see the modified rejections below.

Claim Rejections -35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-14, 17-19, 22, 27-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oshlack et al. (US Pg-Pub 2003/0229111) in view of Kuczynski et al. (US Patent 5,866,164).

Oshlack et al. teach pharmaceutical compositions comprised of naltrexone in amounts of no greater than 0.01 mg and less than 20 mg (paragraph 0016). Table 20A exemplifies a composition comprising naltrexone hydrochloride in an amount of 0.5 mg and hydrocodone bitartrate in an amount of 5 mg, which falls within the claimed ratio of claim 1 (paragraph 0035). Table 20A teaches a composition comprising 0.5 mg of naltrexone and 5 mg of hydrocodone, meeting the limitation of claim 2. Tables 22A, 23A, 24A, 25A, 26A and 27A exemplify a composition comprising naltrexone hydrochloride in an amount of 0.125 mg and hydrocodone bitartrate in amount of 5 mg, which meets the limitation of claims 3-5 (meeting the limitation of "about" 7.5 mg hydrocodone). It is further taught that the composition has a sustained release coat and this is accomplished with Eudragit RS30D (see Tables 9A, 10A, 11A, 12A, 13A). The examples associated with Tables 20, 22-27 all teach a process of making the compositions of the invention within the claimed ratio.

Oshlack et al. does not teach compositions with the exact amounts of naltrexone and hydrocodone as listed in claims 2-11 and 30-34 in one composition or an osmotic dosage form.

Kuczynski et al. teaches osmotic dosage forms comprising hydrocodone and naltrexone (see Examples 1 and 4 and claim 1).

It is obvious to vary and/or optimize the amount of hydrocodone and naltrexone provided in the composition, according to the guidance provided by Oshlack et al., to provide a composition having the desired properties such as the desired concentrations of hydrocodone and naltrexone. It is noted that “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). One would be motivated to optimize the amounts of naltrexone and hydrocodone as taught by Oshlack et al. in order to provide maximal pain relief because Oshlack et al. teach ranges of each drug that overlap with the claimed ranges. One would be motivated to formulate the composition in an osmotic dosage form according to the teachings of Kuczynski et al. to ensure delivery of a therapeutically effective dose at a controlled rate over a sustained period of time and to prevent opioid abuse (Col. 8, lines 20-35).

Claims 1-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherman et al. (US Pg-Pub 2003/0191147) in view of Kaiko et al. (US PgPub 2003/0031712) and Kuczynski et al. (US Patent 5,866,164).

Sherman et al. teach compositions comprised of naltrexone hydrochloride in amounts of about 0.1 to less than about 0.5 mg (paragraphs 0058 and 0065). Paragraphs 0062-0063 exemplify the dose amounts of naltrexone contemplated by the invention and conclude to say that any minimum amount and any maximum amount within range of amounts is possible (paragraph 0064). The composition is taught as

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also having another ingredient in the way of an opioid agonist such as hydrocodone bitartrate (paragraph 0068 and Example 15). Example 15 exemplifies the two compounds in a composition that falls within the claimed ratio. Paragraphs 0242-0251 exemplify a study in which the composition of the invention was tested in methods of treating pain. Further controlled release compositions are also contemplated by Sherman et al. (paragraph 0145). Sherman et al. further teaches that in preparing a composition, amounts of naltrexone at 0.1 % and hydrocodone at 10% are added into a mixture before granulation in Example 15, meeting the limitation of the claimed ratio. Sherman further teaches that other active pharmaceutical ingredients such as ibuprofen (paragraph 0069). Sherman teaches oral dosage forms of the compositions (paragraphs 0070-0071). Sherman teaches the state of the art regarding opioid antagonists being manufactured to prevent abuse of opioid agonists (paragraph 0056).

Sherman et al. does not teach the exact amounts of naltrexone and hydrocodone as listed in claims 2-11 in one composition or that the compositions are interdispersed with a sustained release excipient or an osmotic dosage form.

Kaiko et al. teaches formulations comprising hydrocodone and naltrexone (paragraph 0072) can comprise coatings and melt extrusion multiparticulates that aid in releasing the drug over a twelve to twenty-four hour period to provide analgesia (paragraph 0099). Kaiko discusses that opioid antagonists typically block or reverse all of the effects of opioid agonists and that a use of opioid antagonists is as a once-a-day treatment of naltrexone to block the euphoric affects that might otherwise be obtained upon administration of opioids to addicts (paragraph 0011). Kaiko teaches

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incorporating the opioid agonist and the opioid antagonist into a dosage form that includes a sustained release carrier such that the oral dosage form can be administered on a twice-a-day or once-a-day basis (paragraph 0046).

Kuczynski et al. teaches osmotic dosage forms comprising hydrocodone and naltrexone (see Examples 1 and 4 and claim 1).

Furthermore, it is obvious to vary and/or optimize the amount of naltrexone and hydrocodone provided in the composition, according to the guidance provided by Sherman et al., to provide a composition having the desired properties such as the desired concentrations of both drugs in an effort to provide maximal pain relief. It is noted that “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Accordingly, one of ordinary skill in the art at the time of the invention would have found it obvious to combine the teachings of Sherman et al. which teaches pharmaceutical compositions and methods of making and using such compositions that are comprised of hydrocodone and naltrexone with the teachings of Kaiko et al. which teach similar compositions in which the drugs are interdispersed with sustained release excipients and Kuczynski et al. which teaches osmotic dosage forms comprised of hydrocodone and naltrexone. One would be motivated to do so in an effort to treat pain over a maximal period of time, to increase patient compliance and to reduce the abuse potential of the opioid agonist.

Conclusion

No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

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/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627